

**2. RESPONSE/REMARKS**

**2.1 STATUS OF THE CLAIMS**

*Claims 1-59 were pending at the time of the Action.*

*Claims 2, 3, 5-13 and 43-57 have been withdrawn from consideration.*

*Claims 1 and 4 have been amended herein.*

*Claims 1, 4, 14-42 and 58-59 remain pending in the Application.*

*Applicants note for the record that no rejections were raised against claim 58 and 59, and as such, these claims should now be considered allowable.*

**2.2 APPLICANTS AGAIN REQUEST RECONSIDERATION UNDER 37 C. F. R. § 1.143**

Pursuant to 37 C. F. R. § 1.143, which states in pertinent part:

If the applicant disagrees with the requirement for restriction, he may request reconsideration and withdrawal or modification of the requirement, giving the reasons therefor. In requesting reconsideration the applicant must indicate a provisional election of one invention for prosecution, which invention shall be the one elected in the event the requirement becomes final. The requirement for restriction will be reconsidered on such a request. If the requirement is repeated and made final, the examiner will at the same time act on the claims to the invention elected.

Applicants again request the Examiner's attention to the following pertinent part of M. P. E. P. § 806.04:

“Where an application includes claims directed to different embodiments or species that could fall within the scope of a generic claim, restriction between the species may be proper if the species are independent or distinct. However, 37 C. F. R. §1.141 provides that an allowable generic claim may link a reasonable number of species embraced thereby.

The practice is set forth in 37 C. F. R. § 1.146,” which reads as follows:

“In the first action on an application containing a generic claim to a generic invention (genus) and claims to more than one patentably distinct species embraced thereby, the examiner may require the applicant in the reply to that

action to elect a species of his or her invention to which his or her claim will be restricted if no claim to the genus is found to be allowable. However, if such application contains claims directed to more than a reasonable number of species, the examiner may require restriction of the claims to not more than a reasonable number of species before taking further action in the application.”

## **2.3 APPLICANTS GIVE CONSTRUCTIVE NOTICE OF THEIR RIGHT TO PETITION**

### **UNDER 37 C. F. R. § 1.144**

Since the Examiner has now made a final requirement for restriction, despite Applicants’ earlier arguments against the same, despite Applicants’ request for vacation of further restriction and imposition of species election, and despite Applicants’ formal request herein for Reconsideration, Applicants hereby give constructive notice of their right to Petition the final holding of restriction to the Group Director pursuant to 37 C. F. R. § 1.144. As provided by the Rule, Applicants currently defer petition until after final action or allowance of the claims provisionally elected.

## **2.4 THE OBJECTION TO CLAIMS 4 AND 5 IS OVERCOME.**

*The Action at page 5 objected to claims 4 and 5 as allegedly reciting to non-elected subject matter.*

Applicants respectfully traverse. However, in order to pass claims directed to particular aspects of the invention to issue, Applicants have amended claims 4 and 5 commensurate in scope with the restriction requirement, and as such, should now be allowable based upon the Examiner’s remarks on page 6 of the Action.

Applicants now respectfully request that the objection be withdrawn.

## **2.5 A TERMINAL DISCLAIMER IS SUBMITTED**

***The Action at pages 5-9 rejected claims 1 and 14-42 allegedly on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-3, 9-15, 17-20, and 22-38 of U.S. Patent 6,225,291.***

To render the issue moot, Applicants have submitted a terminal disclaimer in view of commonly co-owned patent 6,225,291, to the extent that the Examiner would be persuaded to enter such a provisional obviousness-type double patenting rejection on any of the pending and newly-added claims. Applicants are mindful of economic concerns and patent term considerations, and therefore submit this disclaimer voluntarily in an effort to secure speedy allowance of all pending claims.

After entry of the paper, Applicants respectfully request now that the objection be withdrawn.

## **2.6 THE REJECTION OF CLAIMS UNDER 35 U. S. C. §112, 1<sup>ST</sup> PARAGRAPH, IS OVERCOME.**

***The Action at pages 8-11 rejected claims 1 and 14-42 under 35 U. S. C. § 112, 1<sup>st</sup> paragraph, allegedly as failing lacking written description.***

Applicants respectfully traverse. Without acquiescing in any way with the propriety or substance of the rejection, however, and solely in view of the now-final Requirement for Restriction, and mindful of patent term and the potential costs of a protracted prosecution, Applicants have clarified the language of claim 1 to recite a population of ribozymes that are specific for an mRNA encoding an IGF-I receptor polypeptide. It is clear from the Specification (particularly on pages 76-78 and Tables 7 and 8), that Applicants had possession of at least two genera of ribozymes that are specific for the IGF-I receptor polypeptide at the time of the invention. The experimental details provided in Example 7 of the Specification also clearly

provide even *further* evidence that the Applicants were in fact, in possession of the claimed invention.

Particularly, in SEQ ID NO:88 and SEQ ID NO:89, Applicants provide specific written description of two particular ribozyme target sequences within the mRNA sequence encoding an IGF-I polypeptide that can serve as a site for cleavage of such an mRNA using an appropriately-specific ribozyme molecule. Likewise, Applicants have further provided specific written description in SEQ ID NO:100 and SEQ ID NO:101, which are two representative ribozyme molecules that can specifically cleave such an IGF-I-specific mRNA.<sup>1</sup>

Applicants assert that this information, when taken in view of the teachings of the entire Specification, would certainly convey to one of skill in the art, the means for making and using ribozymes that target mammalian IGF-I receptor-encoding mRNAs, and that one of skill in the art would be able to prepare and use other ribozymes that would similarly function to cleave the selected mRNA target sequence(s).

Applicants believe that the cited claims are now free from rejection under this section of the Statute, and respectfully requests that the rejection be withdrawn.

## **2.7 THE REJECTION UNDER 35 U. S. C. § 102(A) IS OVERCOME.**

***The Action at pages 11-13 rejects claims 1, 14, 30-34, and 36-39 under 35 U. S. C. § 102(a), allegedly as being anticipated by Caballero et al.***

Applicants respectfully traverse.

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<sup>1</sup>Because SEQ IDNO:s 88 and 89 identify two specific target sequences within the IGF-I receptor-encoding mRNA, and further identify two specific ribozyme sequences that target those sequences (SEQ ID NO:100 and SEQ ID NO:101), Applicants previously argued for reconsideration of the instant Restriction Requirement. Applicants assert that the four sequences are properly considered in the present application. Applicants respectfully request that the two additional IGF-I receptor-specific sequences now be rejoined. Applicants have amended claims 1 and 5 to that end.

To anticipate a claim under Section 102(a), a reference must teach each and every element of the claim. The reference by Caballero fails to do that, and as such, the rejection should be withdrawn.

Caballero in fact, does not recite any specific mRNA sequence(s), and also does not recite any particular ribozyme sequence(s) that would specifically cleave an IGF-I receptor polypeptide-encoding mRNA. Since the present claims recite particular target sequences for the ribozyme (SEQ ID NO:100 and SEQ ID NO:101), as well as specific ribozyme sequences (SEQ IDNO:88 and SEQ ID NO:89), the reference fails to anticipate the claimed invention.

Applicants respectfully request, therefore, that the rejection be withdrawn.

## **2.8 THE REJECTION UNDER 35 U. S. C. § 102(E) IS OVERCOME.**

*The Action at pages 12-13 rejects claims 1, 14, 30-34, and 36-39 under 35 U. S. C. § 102(e), allegedly as being anticipated by Pavco et al. (U.S. Patent 6,346,398).*

Applicants respectfully traverse. As stated above, to anticipate a claim under Section 102(e), the cited reference must teach each and every element of the claim. The patent to Pavco clearly fails to do that, and as such, this rejection should be withdrawn.

Pavco in fact, does not recite specific mRNA target sequence(s) in an mRNA that would encode a mammalian IGF-I receptor polypeptide. The references also does not recite specific ribozyme sequences that would cleave such mRNAs. As stated above, since the present claims recite particular target sequences for the ribozyme (SEQ ID NO:100 and SEQ ID NO:101), as well as specific ribozyme sequences (SEQ IDNO:88 and SEQ ID NO:89), the reference fails to anticipate the claimed invention.

Applicants now respectfully request that the rejection be withdrawn.

**2.9 THE REJECTIONS OF CLAIMS UNDER 35 U. S. C. § 103(A) ARE OVERCOME.**

*The Action at pages 13-15 rejects claims 1, 9, 14-16, 30-32, 36-37, and 39-41 under 35 U. S. C. § 103(a), allegedly as being obvious over Wraight et al. (WO 00/78341) and Thompson et al. (U.S. Patent No. 5,750,390).*

*The Action at pages 16-18 rejects claims 1, 9, 14-16, 30-32, 36-37, and 39-41 under 35 U. S. C. § 103(a), allegedly as being obvious over Pavco et al. in view of Kido et al.*

A finding of obviousness under 35 U. S. C. § 103 requires a determination of the scope and content of the prior art, the level of ordinary skill in the art, the differences between the claimed subject matter and the prior art, and whether the differences are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. John Deere Co.*, 148 USPQ 459 (U.S. S.Ct. 1966).

The relevant inquiry is whether the prior art suggests the invention and whether the prior art would have provided one of ordinary skill in the art with a reasonable expectation of success. *In re O'Farrell*, 7 USPQ 2d 1673 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success *must be founded in the prior art* and not in the Applicant's disclosure (emphasis added) *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991).

Thus, for the cited combination of references to render the present claims legally obvious under 35 U. S. C. § 103, the references must suggest the particular claimed ribozymes that specifically cleave an IGF-I Receptor Polypeptide-encoding mRNA segment. Moreover, the combination must provide one of ordinary skill in the art with a reasonable expectation of obtaining such ribozymes, as well as rAAV vectors, viral particles, mammalian host cells, and diagnostic and therapeutic kits that comprise such ribozymes or vectors. The combination of references must also suggest the particular mRNA sequences that are targeted by those particular

ribozymes. Absent such information, the combination of references fails to render obvious the claimed invention.

### **2.9.1 THE CITED REFERENCES DO NOT OBIATE THE CLAIMED RIBOZYMES**

On page 13 of the Action, the Office states that “Pavco *et al.* teach a ribozyme targeted to, and specifically cleaves a gene encoding a VEGF mRNA.”

In contrast to the present invention, however, Pavco does not teach or suggest ribozymes and ribozyme target sequences relating to the IGF-I Receptor. Likewise, Pavco does not describe the construction of rAAV viral particles, or even mention any mammalian host cells or diagnostic or therapeutic kits that comprise rAAV-based vectors that encode a catalytic RNA that would specifically cleave a mammalian IGF-I Receptor-encoding mRNA.

The same is true for the reference by Wraight. On Page 14 of the Action, the Examiner states that this reference “teach an antisense oligonucleotide that binds to and inhibits expression of a sequence comprising SEQ ID NO:88.”

The Examiner points out, however, “Wraight does not teach the oligonucleotide is a ribozyme and further does not teach a vector comprising a promoter and a ribozyme, a host cell comprising a ribozyme, a composition or a kit comprising a ribozyme.”

Continuing on page 14 of the Action, the Examiner states “Thompson *et al.* teach ribozyme molecules and teach the enzymatic nature of ribozymes is advantageous over technologies such as antisense technologies.” The Office considers that “it would have been obvious to one of skill in the art to substitute a ribozyme for an antisense molecule, as taught by Thompson *et al.*, to inhibit expression of a gene encoding IGF-I receptor polypeptide-encoding mRNA.”

On page 17 of the Action, the Examiner states, “Kido *et al.* teach use of a viral vector comprising a mouse opsin promoter to direct expression in photoreceptor cells, which comprise rod and cone cells, and directs expression in Mueller cells.” The Office concludes, “It would have been obvious to one of ordinary skill in the art to incorporate the mammalian opsin promoter because Kido *et al.* teach a viral vector comprising an opsin promoter is capable of selectively directing expression of therapeutic genes to photoreceptor cells.”

Applicants respectfully traverse.

These references, either alone, and/or in combination clearly fail to provide the relevant teaching, suggestion, or the expectation of success of achieving the claimed invention. (1) None of the disclosures by Wraight *et al.*, Pavco *et al.*, Thompson *et al.*, and/or Kido *et al.*, provides any guidance about selecting particular ribozyme target sequences from within an mRNA sequence that encodes a mammalian IGF-I receptor polypeptide. (2) None of the references teach or suggest the actual target sequences or any such target sequences within the IGF-I receptor-encoding mRNA; (3) None of the references teach or suggest the use of such specific target sequences within the mRNA that encodes the IGF-I Receptor polypeptide in creating specific ribozymes that effectively catalyze the specific cleavage of such target sights; and (4) None of these references teach or suggest *particular ribozyme sequences* that would specifically cleave any such mRNAs, including, for example, those sequences disclosed in the present application (*e.g.*, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:100, and SEQ ID NO:101).

As such, these references cannot render the claimed invention obvious. There is simply no teaching, suggestion, or expectation of success in identifying specific nucleotide sequences within an IGF-I Receptor-specific mRNA, nor is there any teaching, suggestion, or expectation of success of using such identified nucleotide sequences to construct ribozyme molecules that specifically cleave such selected target sequences. There is no motivation to combine the



references to achieve the invention, and there certainly are no IGF-I Receptor-specific target sequences or ribozyme sequences such as those set forth in SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:100, and SEQ ID NO:101.

As such, Applicants respectfully request that the rejection be withdrawn.

## **2.10 APPLICANTS RENEW REQUEST FOR REJOINDER OF THE GROUP II INVENTION**

### **UPON ALLOWANCE OF THE GROUP I INVENTION**

Applicants again note for the record that under the current Statutes, and consistent with the C. F. R., the M. P. E. P, and Technology Center 1600 restriction training materials, if the compositions of the Group I restriction are elected for prosecution, then the subject matter of the Group II invention (directed to *methods of using the compositions of Group I*), is subject to rejoinder upon the allowance of the corresponding composition claims. As such, Applicants again state their affirmative intention to seek rejoinder of the “process for using” claims upon allowance of claims directed to the products claimed in the Group I invention. Referring to the pertinent part of M. P. E. P. § 821.04(b):

“Where claims directed to a product and to a process of making and/or using the product are presented in the same application, applicant may be called upon under 35 U. S. C. § 121 to elect claims to either the product or a process....(T)he claims to the non-elected invention will be withdrawn from further consideration under 37 C. F. R. § 1.142....(H)owever, if applicant elects a claim(s) directed to a product which is subsequently found allowable, withdrawn process claims which depend from or otherwise require all the limitations of an allowable product claim will be considered for rejoinder. All claims directed to a non-elected process invention must depend from or otherwise require all the limitations of an allowable product claim for that process invention to be rejoined. Upon rejoinder of claims directed to a previously non-elected process invention, the restriction requirement between the elected product and rejoined process(es) will be withdrawn.” (emphasis added).

Thus, by constructive election of the products of the Group I invention for initial prosecution on the merits, Applicants again affirmatively state their intention of requesting proper

rejoinder of claims directed to a process of using such compositions (*i.e.*, the subject matter of the Group II invention) upon allowance of the subject matter of the Group I invention.

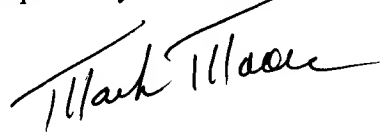
## **2.11 REQUEST FOR EXAMINER/PRACTICE SPECIALIST INTERVIEW**

Applicants hereby request an interview with the Examiner and a TC1600 Practice Specialist *before the issuance of a subsequent Office Action* on the merits to specifically address any particular issues that may remain after consideration of the present paper and entry of the foregoing amendment. Applicants would appreciate the scheduling of such a conference at the Examiner's earliest convenience.

## **2.12 CONCLUSION**

Applicants believe this to be a complete and timely response to the referenced Action, and that all claims are fully supported and patentable under all sections of the Statutes. As such, a Notice of Allowance and Issue Fee Due is respectfully sought from the Office in response to the present submission. Should the Examiner have any questions, or require anything further, a telephone call to the undersigned Applicants' representative would be welcome.

Respectfully submitted,



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